Journal of the Formosan Medical Association (2012) 111, 14–18

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

Risk factors for nasal carriage of methicillin-resistant *Staphylococcus aureus* among patients with end-stage renal disease in Taiwan

Cheng-Yi Wang [a], Vin-Cent Wu [b], Wei-Jie Wang [c], Yu-Feng Lin [b], Yen-Hung Lin [b], Yung-Ming Chen [b], Chi-Ting Su [b], Jen-Yu Wang [a], Kwan-Dun Wu [a], Po-Ren Hsueh [b,*]

[a] *Department of Internal Medicine, Cardinal Tien Hospital, Fu-Jen Catholic University, Taipei, Taiwan*
[b] *Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan*
[c] *Department of Internal Medicine, Tao-Yuan General Hospital, Tao-Yuan, Taiwan*

Received 27 April 2010; received in revised form 26 July 2010; accepted 9 September 2010

KEYWORDS
end-stage renal disease;
ESRD;
methicillin-resistant;
Staphylococcus aureus;
methicillin-susceptible;
MRSA;
MSSA;
nasal colonization

Background/Purpose: Patients with end-stage renal disease (ESRD) are at particular risk for methicillin-resistant *Staphylococcus aureus* (MRSA) infections, especially via nasal colonization of MRSA. Surveillance cultures are recommended to identify patients colonized by MRSA.
Methods: Clinical data and screening cultures of *S. aureus* from the anterior nares of 541 patients on long-term dialysis in the hospitals were performed in March 2007. The follow-up survey was conducted 1 year later.
Results: A total of 32 (5.9%) of the 541 patients were positive nasal cultures for MRSA, while 89 (16.5%) were positive for methicillin-susceptible *S. aureus* (MSSA). In a multivariate analysis, risk factors for ESRD patients with MRSA colonization included congestive heart failure, nursing home admission, and nasogastric tube feeding in the last 3 months. Follow-up of the 32 MRSA colonized patients showed that one (3.1%) died due to MSSA and three (9.3%) died due from MRSA infection.
Conclusions: We found that patients with ESRD and MRSA nasal colonization were associated with a history of congestive heart failure, nursing home admission, and nasogastric tube feeding in the last 3 months.

* Corresponding author. Department of Laboratory Medicine and Internal Medicine, National Taiwan University College of Medicine, 7 Chung-Shan South Road, Taipei, Taiwan.
E-mail address: hsporen@ntu.edu.tw (P.-R. Hsueh).

0929-6646/$ - see front matter
doi:10.1016/j.jfma.2012.01.001

Introduction

Infection is one of the most common causes of hospitalization, morbidity, and mortality among patients with end-stage renal disease (ESRD). Gram-positive cocci, especially *Staphylococcus aureus*, are the most frequently associated microorganisms in long-term dialysis patients and the anterior nares are the most common sites. From here, *S aureus* colonizes and infects other parts of the body, including vascular access sites.[1,2] Recognition and isolation of persons either colonized or infected with methicillin-resistant *S aureus* (MRSA) is recommended to minimize its spread in hospitals. Recent guidelines published by the Society for Healthcare Epidemiology of America (SHEA) recommend surveillance cultures at the time of admission for patients with high risk of MRSA.[3]

Although the risk factors for MRSA colonization in the general population have been well studied,[4,5] there are limited data in ESRD patients, especially in Taiwan. Lederer and colleagues[6] found that MRSA colonization is associated with gender, duration of dialysis, diabetes, malignancy, and exposure to health care (i.e., dialysis staff, hospitalization), while Johnson and others[7] has shown that dialysis patients colonized with MRSA and MSSA were not different from each other. Other studies show that MRSA colonization is more related with patient habits, such as hygiene, bathing frequency, and antibacterial soap use.[8,9] Nonetheless, the prevalence rate of MRSA colonization in dialysis patients in Taiwan[10,11] is not as high as reported in other countries.[7–9]

MRSA infections among dialysis patients are considered to be healthcare associated (HCA) and infecting strains in this population more closely resemble HCA MRSA strains, which are typically staphylococcal cassette chromosome (SCC)*mec* types I and III that lack genes for the Panton-Valentine leukocidin (PVL) toxin. However, our previous study has shown that colonized strains in this population more closely resemble community-associated (CA) MRSA. CA-MRSA strains are more susceptible to antimicrobials than HCA-MRSA isolates and carry the SCC*mec* types IV or V complex and PVL genes.[10]

The study aimed to determine differences in risk factors and prognosis in emergence of CA-MRSA colonization in ESRD patients. The objective was to find risk factors with more details in exposure and demographic characteristics. Specifically, it sought to investigate and compare long-term outcomes of ESRD patients with MRSA nasal carriage and those with methicillin-susceptible *S aureus* (MSSA) nasal carriage.

Patients and methods

Study hospitals and patients

To cover a large area of Taiwan, the study was conducted in three hospitals: National Taiwan University Hospital (NTUH), a 2000-bed tertiary medical center in northern Taiwan; Taoyuan General Hospital, an 800-bed secondary local hospital located in the central part of Taiwan; and the NTUH Yun-Lin Branch, a 400-bed secondary local hospital in southern Taiwan. The NTUH Institutional Review Board approved this study.

During the first 2 weeks of March 2007, specimens for culture were obtained from the anterior nares of outpatients undergoing long-term dialysis in the study hospitals. Patients who were previously admitted to a hospital or those who underwent surgery in the recent one month were excluded. Part of the information on these patients were reported elsewhere.[10,11]

Data collection

Each patient completed a questionnaire investigating a wide variety of possible exposures and demographic characteristics that are classically associated with MRSA.[8,9] Data on hygiene, bathing frequency, antibacterial soap use, and other habits or exposures were also collected using a Likert-type scale (e.g., bathing/showering more than once daily to bathing/showering less than once per week) developed by Miller and colleagues.[9]

Culture of samples from the anterior nares

Samples were obtained for culture using culture swabs (Becton-Dickinson, Sparks, MD, USA) that were plated on mannitol salt plates (Becton-Dickinson) at 35°C for 24 hours. Yellow colonies were streaked on blood agar plates (Becton-Dickinson) and incubated at 35°C for 24 hours. The isolates were identified as *S aureus* using the Staphyloslide agglutination test (Becton-Dickinson). Oxacillin susceptibility was performed by assessing growth on Mueller-Hinton agar with 4% NaCl and 6 μg/mL oxacillin at 35°C for 24 hours according to Clinical and Laboratory Standards Institute (CLSI) guidelines.[12,13] The second swab was processed and tested using the Becton-Dickinson GeneOhm MRSA assay according to the manufacturer's instructions.

Case-control study

A case-control study was performed to identify risk factors for MRSA colonization. Cases were defined as patients with a positive nasal culture for MRSA colonization, while controls were defined as patients with a negative nasal culture for MRSA and had neither positive nor negative results for colonization with MSSA.

Follow-up survey

The follow-up survey was conducted in March 2008, a year after the initial culture of samples from the anterior nares of patients. Infection was defined as local or systemic inflammation and positive pathogen culture results (i.e., sputum, urine, or blood culture). Positive clinical symptoms or signs only but negative culture results were not regarded as an infection. Patient conditions, etiology of death, history of infection in the last 1 year, pathogens of the infection, and such factors were recorded.

Statistical analysis

Results are expressed as mean ± standard deviation unless otherwise specified. The unpaired Student's *t* test was used

to analyze continuous data, and either the χ^2 test or Fisher's exact test was used to analyze categorical data. Statistical analyses were performed with SPSS for Windows version 10.0 (SPSS Inc, Chicago, IL, USA). The binomial test of proportions was used to compare incidences between groups. For other between-group comparisons, Fisher's exact test was used for categorical values, and Student's *t* test or Mann-Whitney U test was used for mean values. A *p* value of less than 0.05 was considered statistically significant.

Results

Of the 541 cultures obtained, 32 (5.9%) were positive for MRSA by culture method, 89 (16.5%) were positive for MSSA, and 420 (77.6%) were culture negative. MRSA accounted for 32 (26.4%) of 121 *S aureus* isolates. The demographic and clinical characteristics of patients with and those without MRSA colonization were shown in Table 1.

Table 1 Characteristics of patients on long-term hospital-based hemodialysis and Risk factors for nasal colonization with MRSA (Univariate analysis).

Characteristic	All patients (*N = 541*)	With MRSA colonization (*n = 32*)	Without MRSA colonization (*n = 509*)	OR (95% CI)	*p* value
Demographic characteristic					
Age, yr					
Mean ± SD	62 ± 14	64 ± 14	62 ± 14	1.008 (0.982–1.035)	0.537
Sex					
Men (*N*, %)	272 (50.3)	15 (46.9)	257 (50.5)	0.87 (0.42–1.77)	0.691
Women (*N*, %)	269 (49.7)	17 (53.1)	252 (49.5)		
Underlying condition					
Diabetes (*N*, %)	203 (37.5)	16 (50.0)	187 (36.7)	1.72 (0.84–3.52)	0.133
COPD (*N*, %)	12 (2.2)	1 (3.1)	11 (2.2)	1.46 (0.18–11.68)	0.720
Congestive heart failure (*N*, %)	118 (21.8)	14 (43.8)	104 (20.4)	3.03 (1.462–6.29)	0.002
Long-term bed ridden (*N*, %)	13 (2.4)	2 (6.3)	11 (2.2)	3.02 (0.64–14.24)	0.143
Acne (*N*, %)	40 (7.4)	5 (15.6)	35 (6.9)	2.51 (0.91–6.91)	0.067
Folliculitis (*N*, %)	30 (5.5)	1 (3.1)	29 (5.7)	0.53 (0.07–4.05)	0.537
Cellulitis (*N*, %)	5 (0.9)	1 (3.1)	4 (0.8)	4.07 (0.44–37.54)	0.18
Nursing home admission (*N*, %)	2 (0.4)	1 (3.1)	1 (0.2)	16.36 (1.00–267.72)	0.008
Previous hospitalization (*N*, %)	108 (20)	5 (15.6)	103 (20.2)	0.73 (0.27–1.94)	0.527
Previous MRSA (*N*, %)	13 (2.4)	1 (3.1)	12 (2.4)	1.33 (0.17–10.59)	0.785
Exposure					
Itching score					0.616
Mean ± SD	5.48 ± 6.32	4.94 ± 4.96	5.52 ± 6.40	0.985 (0.926–1.046)	
Median (range)	4 (0–39)	4 (0–25)	4 (0–39)		
Hygiene score					0.177
Mean ± SD	5.4 ± 2.3	5.9 ± 2.5	5.3 ± 2.3	1.092 (0.960–1.242)	
Median (range)	4 (3–16)	5 (4–13)	4 (3–16)		
Bathing score					0.586
Mean ± SD	4.3 ± 1.2	4.4 ± 1.2	4.3 ± 1.2	1.093 (0.793–1.508)	
Median (range)	5 (1–5)	5 (1–5)	5 (1–5)		
Education score					0.13
Mean ± SD	2.9 ± 1.4	2.5 ± 1.4	2.9 ± 1.4	0.813 (0.620–1.065)	
Median (range)	3 (1-5)	2 (1-5)	3 (1–5)		
NGT feeding in recent 3 months (*N*, %)	13 (2.4)	3 (9.4)	10 (2.0)	5.15 (1.34–19.74)	0.008
Operation in recent 3 months (*N*, %)	52 (9.6)	2 (6.3)	50 (9.8)	0.61 (0.14–2.63)	0.504
Recanalization for AVF/AVG (*N*, %)	43 (8)	3 (9.4)	40 (7.9)	1.21 (0.35–4.15)	0.761
Family members admission in recent 3 months (*N*, %)	31 (6.1)	0 (0)	31 (5.8)	—	0.15
Lives with children (*N*, %)	91 (16.9)	8 (25.0)	83 (16.3)	1.71 (0.74–3.93)	0.204
Lives with children who go to out-of-home day care (*N*, %)	103 (19.1)	5 (15.6)	98 (19.3)	0.78 (0.29–2.06)	0.609
Soap use (*N*, %)	397 (73.7)	20 (62.5)	377 (74.4)	0.58 (0.27–1.21)	0.14
Used public spa, pool, shower (*N*, %)	28 (5.2)	2 (6.3)	26 (5.1)	123 (0.28–5.42)	0.786

AVF = arteriovenous fistula; AVG = arteriovenous graft; CI = confidence interval; COPD = chronic obstructive pulmonary disease; DLC = double lumen catheter; MRSA = methicillin-resistant *Staphylococcus aureus*; NGT = nasogastric tube; OR = odds ratio; WBC = white blood cell.

Patients with MRSA colonization were similar to patients without MRSA colonization in terms of age, sex, presence of diabetes, and other study variables. By univariate analysis, patients with MRSA colonization had congestive heart failure ([CHF] (43.8% vs 20.4%, $p = 0.002$), nursing home admission (3.1% vs 0.8%, $p = 0.008$), and nasogastric tube (NGT) feeding in the last 3 months (9.4% vs 2.0%, $p = 0.008$).

By multivariate analysis (Table 2), factors independently associated with an increased risk of MRSA colonization included CHF (odds ratio [OR], 4.23; 95% confidence interval [CI], 1.86—9.58), nursing home admission (OR, 40.99; 95% CI, 2.19—765.95), and NGT feeding in the last 3 months (OR, 5.29; 95% CI, 1.27—22.02).

Results of the follow-up survey are listed in Table 3. Of the 63 MSSA colonization patients, six (9.5%) had MSSA infection and only one (1.6%) died. Six people (9.5%) had MRSA infection and two (3.2%) died. Of the 32 MRSA colonization patients, one (3.1%) had MSSA infection and died. Four (12.5%) had MRSA infection and three (9.3%) died; two had CHF. No one had either nursing home admission or NGT feeding in the recent 3 months.

Discussion

According to the study of Lederer and colleagues,[6] the prevalence of nasal carriage for *S aureus* is as high as 53%, with 41% MSSA and 12% MRSA. However, in this study, the prevalence of *S aureus* colonization among ESRD patient is 22.4%, with 16.5% MSSA and 5.9% MRSA. This is nearly one-half of those reported by Lederer and colleagues.[6] Nonetheless, there is a fixed ratio of about 4:1 for MSSA and MRSA in both studies. It is interesting to note that the prevalence rate of MRSA colonization in dialysis patients in Taiwan is nearly one-half of those in other countries.

Risk factors previously reported by other studies before had high prevalence of MSSA and MRSA colonization. This study hopes to thoroughly survey possible risk factors for MRSA colonization in ESRD patients in Taiwan, it includes not only basic data and clinical manifestations but also hygiene and educational levels. Conditions that can potentially expose patients to MRSA have been screened, including itching, hygiene, bathing, and education scores, as well as NGT feeding in the last 3 months, soap use, and use of a public spa.

CHF is an independent risk factor for MRSA colonization by multivariate analysis. Chang and colleagues[14] note that MRSA infective endocarditis has a high mortality rate among maintenance hemodialysis patients and that heart failure is a risk factor for mortality from to MRSA infection in these patients. These findings suggest a significant relationship exists between MRSA, CHF, and ESRD. Johnson and others[7] have shown a higher frequency of a history of CHF among those with HCA-MRSA strains. More attention to screening for MRSA colonization or infection in ESRD patients with CHF is therefore warranted.

Other independent risk factors for MRSA colonization in the multivariate analysis are nursing home admission and NGT feeding in the last 3 months. Hidron and colleagues[4] have found that hospitalization in the past 12 months and alternative housing are risk factors for MRSA colonization. Alternative housing includes patients living in personal-care homes, nursing homes, long-term care facilities, and correctional facilities, as well as those who are homeless. Their analysis reveals an elevated rate of MRSA colonization in patients who stayed in hospitals or nursing homes due to medical conditions.

In our previous study,[10] SCC*mec* IV was identified in 13 of 31 (41.9%) MRSA patients and SCC*mec* V was identified in 14 of 31 (45.1%), while total SCCmecs IV or V were identified in 26 of 31 isolates (83.9%). Thus, the prevalence of SCC*mec* IV or V MRSA colonization in ESRD patients is 4.8%. Previously, MRSA infections among dialysis patients were considered to be associated with healthcare. Infecting strains in this population will more closely resemble the HCA-MRSA strains. However, this study shows that colonized strains in this population more closely resembled community-associated MRSA strains.

In conclusion, CHF, nursing home admission, and NGT feeding in the last 3 months are risk factors for nasal MRSA colonization in ESRD patients. Active MRSA surveillance for ESRD patients with such risk factors is crucial for effectively controlling MRSA in hospital hemodialysis settings.

Table 2 Risk factors associated with MRSA colonization in patients on long-term hospital-based hemodialysis (Multivariate analysis).

Risk factor	OR (95% CI)	*p* value
Congestive heart failure	4.23 (1.86—9.58)	0.001
Nursing home admission	40.99 (2.19—765.95)	0.013
Nasogastric tube feeding in the preceding three months	5.29 (1.27—22.02)	0.022

CI = confidence interval; OR = odds ratio.

Table 3 MRSA and MSSA colonizations of patients on long-term hospital-based hemodialysis at 1-year follow-up.

Results	With MSSA colonization (*n = 63*)	With MRSA colonization (*n = 32*)
MSSA infection (*N*, %)	6 (9.5)	1 (3.1)
Expired due to MSSA (*N*, %)	1 (1.6)	1 (3.1)
MRSA infection (*N*, %)	6 (9.5)	4 (12.5)
Expired due to MRSA (*N*, %)	2 (3.2)	3 (9.3)

MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*.

References

1. Salzer W. Antimicrobial-resistant gram-positive bacteria in PD peritonitis and the newer antibiotics used to treat them. *Perit Dial Int* 2005;**25**:313—9.
2. D'Agata EM. Antimicrobial-resistant Gram-positive bacteria among patients undergoing chronic hemodialysis. *Clin Infect Dis* 2002;**35**:1212—8.
3. Calfee DP, Salgado CD, Classen D, Arias KM, Podgorny K, Anderson DJ, et al. Strategies to prevent transmission of

methicillin-resistant *Staphylococcus aureus* in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29**:S62—80.
4. Hidron AI, Kourbatova EV, Halvosa JS, Terrell BJ, McDougal LK, Tenover FC, et al. Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients admitted to an urban hospital: emergence of community-associated MRSA nasal carriage. *Clin Infect Dis* 2005;**41**:159—66.
5. Gorwitz RJ, Kruszon-Moran D, McAllister SK, McQuillan G, McDougal LK, Fosheim GE, et al. Changes in the prevalence of nasal colonization with *Staphylococcus aureus* in the United States, 2001-2004. *J Infect Dis* 2008;**197**:1226—34.
6. Lederer SR, Riedelsdorf G, Schiffl H. Nasal carriage of methicillin resistant *Staphylococcus aureus*: the prevalence, patients at risk and the effect of elimination on outcomes among outclinic haemodialysis patients. *Eur J Med Res* 2007;**12**:284—8.
7. Johnson LB, Jose J, Yousif F, Pawlak J, Saravolatz LD. Prevalence of colonization with community-associated methicillin-resistant *Staphylococcus aureus* among end-stage renal disease patients and healthcare workers. *Infect Control Hosp Epidemiol* 2009;**30**:4—8.
8. Graffunder EM, Venezia RA. Risk factors associated with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection including previous use of antimicrobials. *J Antimicrob Chemother* 2002;**49**:999—1005.
9. Miller LG, Perdreau-Remington F, Bayer AS, Diep B, Tan N, Bharadwa K, et al. Clinical and epidemiologic characteristics cannot distinguish community-associated methicillin-resistant *Staphylococcus aureus* infection from methicillin-susceptible *S. aureus* infection: a prospective investigation. *Clin Infect Dis* 2007;**44**:471—82.
10. Wang CY, Wu VC, Chen YM, Su CT, Wu KD, Hsueh PR. Nasal carriage of methicillin-resistant *Staphylococcus aureus* among patients with end-stage renal disease. *Infect Control Hosp Epidemiol* 2009;**30**:93—4.
11. Lai CC, Wang WJ, Wu VC, Wang CY, Lin YF, Lin YH, et al. Risk factors for methicillin-resistantStaphylococcus aureus colonization among elderly patients with end-stagerenal disease in Taiwan. *Am J Infect Control* 2010;**38**:499—500.
12. Clinical and Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial disk susceptibility tests*. 9th ed. Wayne, PA: CLSI; 2006. Approved standard M2—A9.
13. Clinical and Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing; seventeenth informational supplement*. Wayne, PA: CLSI; 2007. M100—S17.
14. Chang CF, Kuo BI, Chen TL, Yang WC, Lee SD, Lin CC. Infective endocarditis in maintenance hemodialysis patients: fifteen years' experience in one medical center. *J Nephrol* 2004;**17**: 228—35.